AMENDMENTS TO THE CLAIMS/LISTING OF CLAIMS

Please amend claims 21-23, 27-30, 49, 52-56, 60, 63-65, 67-71, 73 and 74 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application:

1 – 20. (Cancelled)

21. (Currently amended) A method for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method consisting ~~essentially~~ of the sequential steps of

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins;

(b) optionally ~~binding said target protein(s) to a solid support~~ removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;

(c) proteolyzing said active target protein(s) to produce a product mixture;

(d) optionally binding said proteolyzed target protein(s) to a solid support;

(e) separating said product mixture into two or more components, one or more of which consist essentially of peptides bound to said probe; and thereafter

([[e]] f) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

22. (Currently amended) A method according to claim 21, wherein said ~~separating step (d)~~ solid support consists essentially of ~~sequestering one or more peptides bound to said probe using~~ a receptor that specifically binds to said probe.

23. (Currently amended) A method according to claim 22, wherein said probe consists essentially of a functional group, a detectable label, an optional affinity group, and an

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optional linking group, and said receptor is avidin, streptavidin, or an antibody or fragment thereof that binds to said detectable label.

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24. (Previously presented) A method according to claim 23, wherein said detectable label consists essentially of a fluorescent moiety, and said signal is a fluorescent signal generated from said probe.

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25. (Original) A method according to claim 21, wherein said signal is a mass spectrum.

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26. (Previously presented) A method according to claim 21, wherein, prior to said proteolyzing step (c), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

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27. (Currently amended) A method according to claim 21, wherein said probe consists essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, and said detectable label is selected from the group consisting of a fluorescent moiety and ~~an isotopic label~~ biotin.

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28. (Currently amended) A method according to claim 21, wherein said separating step ([[d]] e) is selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry, MALDI mass spectrometry and combinations thereof.

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29. (Currently amended) A method according to claim [[21]] 26, wherein ~~prior to said proteolyzing step (c),~~ said one or more active target proteins bound to said probe are bound to a solid support, thereby facilitating said removing step (b).

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30. (Currently amended) A method ~~according to claim 21, wherein said method further consists essentially of~~ for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method consisting of the sequential steps of

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins;

(b) optionally adding one or more standard proteins to said complex protein mixture prior to [[said]] proteolysis step ([[c]] d), wherein said standard protein(s) are optionally labeled with an activity based probe prior to addition to said complex protein mixture;

(c) optionally removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;

(d) proteolyzing said active target protein(s) to produce a product mixture;

(e) optionally binding said proteolyzed target protein(s) to a solid support;

(f) separating said product mixture into two or more components, one or more of which consist essentially of peptides bound to said probe; and thereafter

(g) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

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31. (Original) A method according to claim 30, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

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32. (Previously presented) A method according to claim 31, wherein said standard protein(s) are labeled with an activity based probe consisting essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, wherein said detectable label is distinguishable from said activity based probe contacted with complex protein mixture.

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33 – 47. (Cancelled)

48. (Previously presented) A method according to claim 21, wherein said complex protein mixture is a proteome.

49. (Currently amended) A method for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method consisting of the sequential steps of ~~comprising~~:

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins, wherein said probe comprises a fluorescent moiety;

(b) optionally removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;

(c) proteolyzing said active target protein(s) to produce a product mixture;

(d) optionally binding said proteolyzed target protein(s) to a solid support consisting essentially of an antibody or fragment thereof that binds to said fluorescent moiety;

([[c]] e) separating said product mixture into two or more components, one or more of which ~~comprise~~ consist essentially of peptides bound to said probe, ~~said probe using a receptor that specifically binds to said probe, wherein said receptor is an antibody or fragment thereof that binds to said fluorescent moiety~~; and thereafter

([[d]] f) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

50. (Previously presented) A method according to claim 49, wherein said signal is a fluorescent signal generated from said probe.

51. (Previously presented) A method according to claim 49, wherein said signal is a mass spectrum.

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~~52.~~ (Currently amended) A method according to claim ~~49~~, wherein, prior to said proteolyzing step ([[b]] c), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

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~~53.~~ (Currently amended) A method according to claim ~~49~~, wherein said probe ~~comprises a~~ consists essentially of a functional group, a detectable label, an optional affinity group, and an optional linking group, and said detectable label is selected from the group consisting of ~~the~~ a fluorescent moiety and ~~an isotopic label~~ biotin.

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~~54.~~ (Currently amended) A method according to claim ~~49~~, wherein said separating step ([[c]] e) comprises one or more separation methods selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry and MALDI mass spectrometry.

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~~55.~~ (Currently amended) A method according to claim ~~49~~, wherein prior to said proteolyzing step ([[b]] c), said one or more active target proteins bound to said probe are bound to a solid support.

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~~56.~~ (Currently amended) A method ~~according to claim 49, wherein said method further comprises~~ for determining the presence, amount, or activity of one or more active target proteins in a complex protein mixture, the method consisting of the sequential steps of

(a) contacting said complex protein mixture with a single activity based probe that specifically binds predominantly to a single target site on one or more active target proteins, wherein said probe comprises a fluorescent moiety;

(b) adding one or more standard proteins to said complex protein mixture ~~prior to [[said]] proteolysis step ([[b]] d)~~, wherein said standard protein(s) are optionally labeled with an activity based probe prior to addition to said complex protein mixture;

(c) optionally removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;

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(d) proteolyzing said active target protein(s) to produce a product mixture;

(e) optionally binding said proteolyzed target protein(s) to a solid support consisting essentially of an antibody or fragment thereof that binds to said fluorescent moiety;

(f) separating said product mixture into two or more components, one or more of which consist essentially of peptides bound to said probe; and thereafter

(g) generating a signal from said peptides bound to said probe, wherein said signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

22 ~~57~~. (Previously presented) A method according to claim ~~56~~ 21, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

23 ~~58~~. (Previously presented) A method according to claim ~~57~~ 22, wherein said standard protein(s) are labeled with an activity based probe comprising the fluorescent moiety that is distinguishable from said activity based probe contacted with complex protein mixture.

24 ~~59~~. (Previously presented) A method according to claim ~~49~~ 19, wherein said complex protein mixture is a proteome.

25 ~~60~~. (Withdrawn; currently amended) A method for comparing the presence, amount or activity of one or more active target proteins in each of two or more discrete proteomes, the method consisting of the sequential steps of ~~comprising~~:

(a) contacting each of said discrete proteomes with a single activity based probe that binds predominantly to a single target site on one or more active target proteins, wherein the same activity based probe is used for each discrete proteome;

(b) optionally removing from each of said discrete proteomes one or more components of said discrete proteome not bound to said probe;

(c) proteolyzing said discrete proteomes to produce a product mixture;

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(d) optionally binding said proteolyzed target protein(s) to a solid support;

([[c]] **c**) separating each of said product mixtures into two or more components, one or more of which comprise peptides bound to said probe; and **thereafter**

([[d]] **f**) comparing the presence, amount or activity of the active target proteins in each of the discrete proteomes by generating a signal from said one or more components comprising peptides bound to said probe.

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~~61.~~ (Withdrawn) The method according to claim ~~60~~ wherein said activity based probe binds specifically to a single target site on one or more active target proteins.

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~~62.~~ (Withdrawn) The method according to claim ~~60~~ wherein said activity based probe covalently binds to a single target site on one or more active target proteins.

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~~63.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein said ~~separating step (c) comprises sequestering one or more peptides bound to said probe using~~ **solid support consists essentially of** a receptor that specifically binds to said probe.

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~~64.~~ (Withdrawn; currently amended) A method according to claim ~~63~~, wherein said probe ~~comprises~~ **consists of** a fluorescent moiety, and said receptor is an antibody or fragment thereof that binds to said fluorescent moiety.

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~~65.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein said probe ~~comprises~~ **consists of** a fluorescent moiety, and said signal is a fluorescent signal generated from said probe.

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~~66.~~ (Withdrawn) A method according to claim ~~60~~, wherein said signal is a mass spectrum.

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~~67.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein, prior to said proteolyzing step ([[b]] c), one or more components of said complex protein mixture not bound to said probe are removed from said complex protein mixture.

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~~68.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein said probe ~~comprises~~ **consists essentially of** a label selected from the group consisting of a fluorescent moiety and a biotin moiety.

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~~69.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein said separating step ([[c]] e) comprises one or more separation methods selected from the group consisting of affinity separation, gel electrophoresis, capillary electrophoresis, liquid chromatography, HPLC, electrospray ionization mass spectrometry, MALDI mass spectrometry and combinations thereof.

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~~70.~~ (Withdrawn; currently amended) A method according to claim ~~60~~, wherein prior to said proteolyzing step ([[b]] c), said one or more active target proteins bound to said probe are bound to a solid support.

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~~71.~~ (Withdrawn; currently amended) A method ~~according to claim 60, wherein said method further comprises~~ **for comparing the presence, amount or activity of one or more active target proteins in each of two or more discrete proteomes, the method consisting of** the sequential steps of

(a) contacting each of said discrete proteomes with a single activity based probe that binds predominantly to a single target site on one or more active target proteins, wherein the same activity based probe is used for each discrete proteome;

(b) adding one or more standard proteins to said complex proteome mixture ~~prior to [[said]] proteolysis step ([[b]] d),~~ **wherein said standard protein(s) are optionally labeled with an activity based probe prior to addition to said complex protein mixture;**

(c) optionally removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;

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(d) proteolyzing said discrete proteomes to produce a product mixture;

(e) optionally binding said target protein(s) to a solid support;

(f) separating each of said product mixtures into two or more components, one or more of which comprise peptides bound to said probe; and thereafter

(g) comparing the presence, amount or activity of the active target proteins in each of the discrete proteomes by generating a signal from said one or more components comprising peptides bound to said probe.

37 (Withdrawn) A method according to claim 36, wherein said standard protein(s) are labeled with an activity based probe prior to addition to said complex protein mixture.

38 (Withdrawn; currently amended) A method according to claim 37, wherein said activity based probe labeling said standard proteins ~~comprises~~ **consists of** a fluorescent moiety that is distinguishable from said activity based probe contacted with complex protein mixture.

39 (Currently amended) A method for detecting the presence, amount or activity of one or more active target proteins in a single complex protein mixture, the method **consisting of** the sequential steps of ~~comprising~~:

(a) contacting said complex protein mixture with an activity based probe that specifically binds predominantly to a single target site on one or more active target protein;

(b) **optionally removing from said complex protein mixture one or more components of said complex protein mixture not bound to said probe;**

(c) proteolyzing said active target proteins to produce a product mixture;

(d) optionally binding said target protein(s) to a solid support;

([[c]] **e**) separating said product mixture into two or more components, one or more of which comprise peptides bound to said probe; and **thereafter**

(([d]) f) generating a signal from said peptides bound to said probe, wherein the signal is correlated to the presence, amount, or activity of said one or more active target proteins in said complex protein mixture.

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